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Two-stage revision of infected knee replacement in patients with antibiotic-loaded spacer

Two-stage treatment of infected total knee arthroplasty

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Abstract
Aim: Prosthetic infections after total knee arthroplasty (TKA) are the most important cause of early failure in TKA, despite advances in diagnosis and treatment. In our study, we aimed to evaluate the results of a two-stage total knee arthroplasty using an antibiotic-loaded spacer.
Material and Methods: Two-stage revision was performed in all patients who were diagnosed with infected TKA. A prefabricated antibiotic-loaded articulating polymethylmethacrylate spacer or a vancomycin + gentamicin-loaded spacer to fill the gap was placed following debridement and irrigation. The patients were evaluated in terms of laboratory, clinical and radiographic findings at postoperative months 1, 3, 6 and in the following months. The recorded American Knee Society (AKS) Knee Scores of the patients before surgery and at the final follow-up were included in the evaluation.
Results: The mean patient age was 71.38 (range: 56-85) years. Culture was positive in 10 (47.6%) and negative in 11 (52.4%) of the 21 patients. The mean time from the most recent surgery (primary or revision) until removal of the prosthetic implant was 30.38 months (range: 0.5-96 months) and the mean time between the first and second stages was 6.2 months (range: 3-16 months). The mean AKS knee score increased from 39.1 points (range: 31-48) prior to the first stage to 74.95 points (range: 63-86) after the second stage ($p<0.001$).
Discussion: The two-step revision arthroplasty technique is a reliable and effective method in the treatment of infected TKA. The use of antibiotic-loaded spacers gives satisfactory results in increasing joint range of motion(ROM).

Keywords
Antibiotic-Loaded Spacer, Periprosthetic Joint Infection, Total Knee Arthroplasty

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Introduction

Primary prosthetic joint infection (PJI) is among the most severe complications after total knee arthroplasty (TKA). It remains to be the most frequently reported cause of early failure in TKA, despite advancements in the prevention, diagnosis and treatment of prosthetic joint infections encountered after TKA [1]. In spite of the widespread use of antibiotic prophylaxis in the preoperative and postoperative periods, improved operating room conditions (such as laminar flow) and preoperative examination of patients for the causes of infection, the rate of PJI after primary total joint replacement ranges between 1-3% [2]. Although rare, primary prosthetic joint infections have a significant impact on patients' quality of life. Rapid diagnosis and identification of the causative agent are of utmost importance in achieving a successful outcome in the treatment of infected TKA. The goal of revision surgery is to eradicate the infection and create a pain-free, functional and stable joint. Majority of patients with prosthetic joint infection require treatment with a single- or two-stage revision surgery. In single-stage revision surgery, thorough irrigation, debridement and reimplantation are performed within a single session. Indications for the use of a single-stage revision in infected knees are as follows: identification of the causative organism, the absence of a polymicrobial infection and availability of sufficient soft and bone tissue. On the other hand, two-stage revision is considered the gold standard in the treatment of infected TKAs. A two-stage revision surgery requires the removal of all indwelling components, radical debridement of the medullary canal and synovial membrane and abundant irrigation. This is followed by placement of an antibiotic-loaded cement or spacer. Prolonged intravenous and oral antibiotic therapy should be administered in the postoperative period [3-5].

This study aimed to evaluate the outcomes of the two-stage revision of infected knee replacement in patients who had an antibiotic-loaded spacer.

Material and Methods

Patients who underwent revision knee replacement between January 2008 and January 2016 in the orthopedics clinic of Ege University were retrospectively evaluated. Thirty five patients had undergone revision knee replacement for various reasons within the specified time interval. Of these patients, 21 underwent a two-stage revision TKA due to infection. Demographic data of the patients and treatment outcomes were retrospectively evaluated. Demographic data including age, gender, affected side and etiology of arthritis as well as joint ROM were evaluated. Growth of the same microorganism in two or more cultures or in intraoperative cultures obtained from the synovial fluid or growth of a virulent microorganism such as S. aureus in one culture or the presence of a sinus tract that communicates with the prosthesis were considered indicators of infection. In patients who did not meet these major criteria, the presence of three of the following five minor criteria was also considered an indicator of prosthetic infection [6].

The five minor criteria are: (I) Elevated Serum Erythrocyte Sedimentation Rate (ESR) and Serum C-Reactive Protein (CRP) concentration (II) Increased White Blood Cell (WBC) count in synovial fluid or a ++ Leukocyte Esterase Strip Test (III) Increased polymorphonuclear neutrophil (PMN) percentage (%) in synovial fluid (IV) Positive histological analysis of periprosthetic tissue (V) A single positive culture.

A two-stage revision was performed in all patients who were diagnosed with infected TKA. A prefabricated antibiotic-loaded articulating polymethylmethacrylate spacer or a vancomycin + gentamicin-loaded spacer to fill the gap was placed following debridement and irrigation. The patients were evaluated in terms of laboratory, clinical and radiographic findings at postoperative months 1, 3, 6 and in the following months. The recorded American Knee Society (AKS) Knee Scores of the patients before surgery and at the final follow-up were included in the evaluation. In this scoring system, a score of less than 60 was considered a poor outcome, a score between 60-69 was considered a fair outcome, a score between 70-84 was considered a good outcome and a score between 85-100 was considered an excellent outcome [7].

Descriptive characteristics were determined. Dependent t-test was used to compare the preoperative and postoperative measurements. $p<0.05$ was considered statistically significant. Informed consent was obtained from each patient. The study protocol was approved by the local ethics committee (Approval number/date 0199/27.04.2023).

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

The mean patient age was 71.38 (range: 56-85) years. The culture was positive in 10 (47.6%) and negative in 11 (52.4%) of the 21 patients. The identified microorganisms in the preoperative and intraoperative cultures were as follows: coagulase-negative staphylococci in 2 patients, methicillin-sensitive Staphylococcus Aureus in 7 patients and Enterococcus Faecalis in 1 patient.

The mean WBC count dropped from 12.200/μL prior to the first stage (range: 9.350-20.600 μL) to 7.150/μL (range: 4.500 -10.910 μL) prior to the second stage. The mean ESR dropped from 75.38 mm/h prior to the first stage (range: 36 -110 mm/h) to 23.57 mm/h prior to the second stage (range: 8-41 mm/h). The mean CRP level dropped from 13.34 mg/dL prior to the first stage (range: 2.94-40 mg/dL) to 0.74 mg/dL prior to the second stage (range: 0.06-3.13 mg/dL).

The mean time from the most recent surgery until removal of the prosthetic implant was 30.38 months (range: 0.5-96 months) and the mean time between the first and second stage was 6.2 months (range: 3-16 months). Nine patients underwent delayed reimplantation after 6 months. The delays were due to cellulitis in three patients, redness in four patients and superficial wound infection in two patients. Ten patients who had positive cultures after the first-stage surgery were treated with intravenous antibiotics to which the organisms that were identified in culture were sensitive. The remaining 11 patients who had negative cultures were administered intravenous or oral cephalosporins.

The mean ROM increased from 52.4° (range: 40°-70°) prior to the first stage to 90° (range: 80°-100°) after the second stage ($p<0.001$). The mean AKS knee score increased from 39.1

points (range: 31-48) prior to the first stage to 74.95 points (range: 63-86) after the second stage ($p<0.001$). The mean AKS function score increased from 14.5 points (range: 5-50) prior to the first stage to 69.76 points (range: 60-75) after the second stage ($p<0.001$). The mean time until partial weight bearing was 5.6 days (range: 2-6 days). According to the clinical examination and results of the blood tests at the final follow-up, 19 patients did not have any findings of infection recurrence, whereas 2 patients (9.5%) required long-term antibiotherapy and repeat debridement due to recurrent infection. Of the 21 patients, 11 (52.4%) had been diagnosed with diabetes mellitus (DM) and 3 had rheumatoid arthritis (RA). One of the two patients who had a recurrent infection and underwent debridement had DM and RA. This patient had a prolonged recurrence of infection.

Discussion

Treatment of infected TKAs is a challenging process. The surgeon treating an infected TKA aims to eradicate the infection and maximize long-term function and quality of life. The two-stage revision TKA is considered the gold standard in achieving these goals. Radical surgical treatments such as arthrodesis, resection arthroplasty and amputation are preferred in the presence of a treatment-resistant infection when the extensor mechanism is destroyed and soft tissue coverage is not sufficient. The timing of reimplantation is of utmost importance for treatment success in two-stage revision TKA [8,9]. Therefore, the proper use of antibiotics and the duration of antibiotherapy should be thoroughly planned after proper irrigation and debridement. Mahmud et al. recommended at least 6 weeks of intravenous antibiotic therapy prior to reimplantation [10]. In making the decision to perform second-stage revision surgery, it is recommended to discontinue antibiotherapy for at least two weeks and perform a knee joint aspiration for culturing and biochemical testing [11,12]. We treated our patients with intravenous antibiotherapy for 6 weeks followed by oral antibiotic therapy for 4 weeks depending on the bacterial growth in culture. We stopped administering antibiotic therapy in the following 2 weeks and performed revision TKA in the presence of 3 consecutively negative CRP tests after IV and oral antibiotherapy, improvement in clinical symptoms and sufficient quality of soft tissue. While Insall et al. recommended performing the second stage when soft tissue is in good condition and joint aspirate does not show any findings of infection, Mont et al. emphasized the importance of preoperative evaluation of sensitivity and cultures through biopsy and joint aspiration [13,14]. On the other hand, other authors have also claimed that the decline in ESR and CRP levels as well as the improvement observed in the clinical examination would suffice without the need for another aspiration, similar to the present study [15]. In terms of treatment success, the rate of infection eradication was 90.4% with the method used in this study. Although it seems like performing joint aspiration and culture prior to the second stage would lead to increased treatment success, it is known that most of the infected TKAs do not even manifest with a positive culture. We believe that the method we used is much more preferable in clinical practice.

A short time interval between the first and second stages would also complicate the eradication of infection in the revision of infected TKAs, thereby leading to an increase in the frequency of of recurrence of infection. On the other hand, a long-time interval between the first and second stages would have a negative effect on joint ROM. In contrast, some studies have also reported an increased rate of recurrent infections with a longer time between the two surgeries [9]. In addition, it is known that a longer time between the two surgeries leads to decreased bone mineral density and a higher degree of muscle atrophy, which both render rehabilitation more difficult after the second stage. More successful outcomes have been obtained in revisions performed after a minimum of 6 weeks [13]. In a study by Hoffman AA et al., they reported a mean time interval of 3 months (1-15 months) between the first and second stages [16]. In the present study, the mean time interval between the two stages was 6.76 months (3-16 months). However, the second stage was delayed in some patients due to several reasons such as the need to ensure that the infection was eradicated in patients who were administered empiric antibiotherapy despite negative cultures and to wait for skin problems to resolve in patients who had an active draining fistula.

The results of a two-stage revision performed on a large series consisting of 253 patients were reported by Mahmud et al. in 2012. It was stated that 16 patients (7%) developed reinfection within a mean follow-up of 48 months. The clinical AKS scores were found to be 60 and 129 before and after surgery, respectively. The rate of infection-free cases following two-stage revision has been reported to be 85% within 5 years and 78% within 10 years [10]. In a study by Haleem et al. conducted with 96 knees of 94 patients, it was reported that implant removal was performed due to reinfection in 9 patients during a mean follow-up of 7.2 years [12]. Freeman et al. studied 76 revision cases in 74 patients, wherein static spacers were used in 28 patients and articulating spacers in 48 patients, wherein the success rates were 92.1% and 94.7%, respectively [17]. In a study by Westrich et al., 75 knees of 72 patients were studied and infection eradication rate was reported to be 90.7%[18]. Two-stage revision procedures performed for antibiotic-resistant organisms were investigated in one study. It was reported that the eradication rate of antibiotic-resistant organisms was 91.2%. In the present study, 2 patients (9.6%) developed reinfection throughout a mean follow-up of 31 months. During follow-up after reimplantation, these two patients who presented with pain, localized heat as well as infection findings, i.e., elevated white blood cell count, ESR and CRP, underwent repeated debridement and received intravenous antibiotics. However, the symptoms did not improve and therefore we had to remove the polyethylene filler with cement and the femoral component implanted in the first stage and perform a second stage to manage the infection.

According to the literature, vancomycin, tobramycin, teicoplanin and gentamicin have been utilized as antibiotics in cement [3,4]. In our patients, we used antibiotic cement prepared with 4g of vancomycin in a cement containing 40 g of gentamicin. None of the patients exhibited toxicity. The infection was eradicated within 3 to 6 months in 13 patients, within 7 months in 4 patients, within 9 months in 1 patient, within 14 months in 1 patient and within 16 months in 1 patient. One patient exhibited a recurrent infection. An extensive debridement should be performed to

eradicate the infection while performing surgery for infected TKA. However, large bone defects can be formed and collateral ligament insufficiency can be observed while removing the implant at this stage. While using a thick cement to fill the void after debridement leads to decreased instability, it also leads to a larger bone defect and increased ligament laxity. These risks would be minimized with the use of antibiotic-loaded cement spacers. On the other hand, use of spacers with proper antibiotics prepared by a surgeon can also lead to similar results. Articulating cement spacers can be preferred to prevent joint contracture and increase ROM, particularly in two-stage revision surgeries. There are studies reporting that articulating spacers provide better functional outcomes compared to static spacers, allowing for early rehabilitation and ROM exercises between the two stages.

In our patients, the clinical AKS knee scores were 39.1 and 74.9 and function scores were 14.5 and 69.8 before the treatment and at the end of follow-up, respectively. There is still no clear consensus on the superiority of articulating and static spacers over one another in the two-stage surgical treatment procedure for infected TKA [19]. Vasarhelyi et al. reported better ROM and AKS scores in 104 patients in whom they used articulating spacers compared to static spacers in a study conducted with 176 patients with PJI [20]. Voleti et al. published a systematic review comparing two types of spacers and reported that there was no significant difference between the spacers in terms of reinfection rates (7% for articulating and 12% for static spacers, p=0.2) or functional scores. They also found that the articulating spacer group had improved ROM (101 vs. 91 degrees, P = 0.002)[21]. Similarly, Pivec et al. conducted a systematic review of 48 studies and reported a higher ROM in the articulating spacer group (100 vs. 92 degrees, p=0.001) [22]. However, there was no difference in terms of reinfection rates or functional scores. The ROM of the joint in our study was significantly increased (p <0.001).

This study had some limitations. First of all, the study was retrospective. Second, it was difficult to perform definitive statistical analyses due to the small sample size of the reinfection group after two-stage reimplantation. There is a need for further multicenter and prospective studies with a larger sample size for clearer results. We do not recommend set diagnostic standards for infection eradication in patients with an infected prosthetic joint. We believe that each patient should be evaluated individually.

Conclusion

Two-stage revision arthroplasty is a reliable and effective technique in the treatment of infected TKA. This procedure enhances treatment success with soft tissue evaluation, culturing and identification of the causative pathogen.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of interest

The authors declare no conflict of interest.

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